

We Claim:

1. A method for the preparation of a recombinant polypeptide comprising
 - a) introducing into a host cell an expression vector comprising:
 - (1) a nucleic acid sequence capable of regulating transcription in a host cell,
5 operatively linked to
 - (2) a chimeric nucleic acid sequence encoding a fusion protein, the chimeric nucleic acid sequence comprising (a) a nucleic acid sequence encoding a pro-peptide derived from an autocatalytically maturing zymogen, linked in
10 reading frame to (b) a nucleic acid sequence heterologous to the pro-peptide and encoding the recombinant polypeptide; operatively linked to
 - (3) a nucleic acid sequence encoding a termination region functional in said host cell,
 - b) growing the host cell to produce said fusion protein; and
 - c) altering the environment of the fusion protein so that the pro-peptide is
15 cleaved from the fusion protein to release the recombinant polypeptide.
2. A method according to claim 1 wherein said pro-peptide is derived from a protease.
3. A method according to claim 1 wherein said pro-peptide is derived from an aspartic protease, a serine protease or a cysteine protease.
- 20 4. A method according to claim 1 wherein said pro-peptide is selected from the group comprising chymosin, trypsinogen, pepsin, HIV-1 protease, pepsinogen, cathepsin or yeast proteinase A.
5. A method according to claim 1 wherein the polypeptide is hirudin or carp growth hormone.
- 25 6. The method according to claim 1 wherein the chimeric nucleic acid sequence does not include a sequence encoding a mature form of the zymogen.
7. A method according to claim 1 wherein the altering the environment comprises altering the pH, altering the salt concentration or altering the temperature.
8. A method according to claim 7 wherein the altering the pH comprises
30 altering the pH to a pH from about 2 to about 4.5.

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9. A method according to claim 1 wherein the altering the environment takes place under *in vitro* conditions.
10. A method according to claim 1 wherein said altering the environment takes place under *in vivo* conditions.
- 5 11. A method according to claim 10 wherein the *in vivo* conditions are those prevalent in a tissue or bodily fluid of an animal.
12. A method according to claim 11 wherein the tissue or bodily fluid comprises the milk, blood, the stomach, the gut or the kidneys of said animal.
- 10 13. A method according to claim 1 wherein a mature form of an autocatalytically maturing zymogen is added in step (c) wherein said zymogen is homologous to the pro-peptide.
14. A method according to claim 1 wherein a mature form of an autocatalytically maturing zymogen is added in step (c) wherein said zymogen is heterologous to the pro-peptide.
- 15 15. The method according to claims 13 or 14 wherein the mature zymogen is added under *in vitro* conditions.
16. The method according to claims 13 or 14 wherein the mature zymogen is added under *in vivo* conditions.
17. The method according to claim 16 wherein said *in vivo* conditions are those
20 prevalent in a tissue or bodily fluid of an animal.
18. The method according to claim 17 wherein the tissue or bodily fluid is a stomach, kidney, gut, blood or milk of said animal.
19. A method according to any one of claims 1 to 18 wherein said nucleic acid sequences are deoxyribonucleic acid (DNA) sequences.
- 25 20. A chimeric nucleic acid sequence encoding a fusion protein comprising (a) a nucleic acid sequence encoding a pro-peptide from an autocatalytically maturing zymogen

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and (b) a nucleic acid sequence encoding a polypeptide that is heterologous to the pro-peptide.

21. A chimeric nucleic acid sequence according to claim 20 wherein the pro-peptide is derived from a protease.

5 22. A chimeric nucleic acid sequence according to claim 20 wherein the pro-peptide is derived from a serine protease, aspartic protease or a cysteine protease.

23. A chimeric nucleic acid sequence according to claim 20 wherein the pro-peptide is derived from chymosin, trypsinogen, pepsin, HIV-1 protease, pepsinogen, cathepsin or yeast proteinase A.

10 24. A chimeric nucleic acid sequence according to claim 20 wherein the polypeptide is hirudin or carp growth hormone.

25. A chimeric nucleic acid sequence according to claim 20 which does not include a sequence encoding a mature form of the zymogen.

15 26. A chimeric nucleic acid sequence according to any one of claims 20 to 25 wherein said nucleic acid sequences are deoxyribonucleic acid (DNA) sequences.

27. A chimeric nucleic acid sequence according to claim 26 wherein the chimeric sequence is as shown in SEQ.ID.NO 1. or SEQ. ID. NO.2.

28. An expression vector comprising a chimeric nucleic acid sequence according to any one of claims 20 to 27 and a regulatory sequence suitable for expression in a host cell.

20 29. A transformed host cell containing an expression vector according to claim 28.

30. A transformed host cell containing an expression vector according to claim 28 wherein the host cell is a bacterial cell, a fungal cell, a plant cell or an animal cell.

25 31. A method of delivering a therapeutic or nutritional polypeptide to a human or animal comprising

(a) providing a fusion protein comprising

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- (i) a pro-peptide derived from an autocatalytically maturing enzyme, linked to
 - (ii) a polypeptide that is heterologous to the pro-peptide and is a therapeutic or nutritional protein; and
- 5 (b) administering the fusion protein to the human or animal where the therapeutic or nutritional polypeptide is cleaved from the pro-peptide.

32. A method according to claim 31 wherein the mature form of an autocatalytically maturing zymogen is added in step (b).

10 33. A method according to claim 31 wherein said mature autocatalytically maturing zymogen is homologous to the pro-peptide.

34. A method according to claim 31 wherein said mature autocatalytically maturing zymogen is heterologous to the pro-peptide.

15 35. A method according to any one of claims 31 to 34 wherein said pro-peptide is derived from a protease.

36. A method according to claim 35 wherein said protease is an aspartic protease, a serine protease or a cysteine protease.

37. A method according to claim 35 wherein said protease is chymosin, trypsinogen, pepsin, HIV-1 protease, pepsinogen, cathepsin or yeast proteinase A.

20 38. A method according to any one of claims 31 to 37 wherein the polypeptide is a vaccine, a peptide antibiotic, a cattle feed enzyme, a cytokine, a gastric lipase or a lactase.

39. A pharmaceutical composition comprising a fusion protein which comprises (a) a pro-peptide derived from an autocatalytically maturing zymogen and (b) a polypeptide that is heterologous to the pro-peptide, in admixture with a suitable diluent or carrier.

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40. A food composition comprising a fusion protein which comprises a pro-peptide derived from an autocatalytically maturing zymogen and (b) a polypeptide that is heterologous to the pro-peptide, in admixture with a suitable diluent or carrier.

41. A pharmaceutical composition comprising a chimeric nucleic acid sequence encoding a fusion protein, the chimeric nucleic acid sequence comprising (a) a first nucleic acid sequence encoding a pro-peptide derived from an autocatalytically maturing zymogen and (b) a second nucleic acid sequence encoding a polypeptide that is heterologous to the pro-peptide.
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42. A food composition comprising a chimeric nucleic acid sequence encoding a fusion protein, the chimeric nucleic acid sequence comprising (a) a first nucleic acid sequence encoding a pro-peptide derived from an autocatalytically maturing zymogen and (b) a second nucleic acid sequence encoding a polypeptide that is heterologous to the pro-peptide.
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43. A composition according to claim 41 or 42 wherein the nucleic acid sequences are deoxyribonucleic acid (DNA) sequences.
44. A composition according to claim 41, 42 or 43 wherein said chimeric nucleic acid sequence does not include a sequence encoding a mature form of the zymogen.
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45. A fusion protein comprising (a) a pro-peptide derived from an autocatalytically maturing zymogen and (b) a polypeptide that is heterologous to the pro-peptide.
46. A fusion protein according to claim 45 which does not include a mature form of the zymogen.
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47. A use of a fusion protein comprising (i) a pro-peptide derived from an autocatalytically maturing enzyme, linked to (ii) a polypeptide that is heterologous to the pro-peptide and is a therapeutic or nutritional protein; to deliver a therapeutic or nutritional protein to a human or animal.